

Atrioventricular node ablation is not a prerequisite for cardiac resynchronization therapy in patients with chronic atrial fibrillation

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Abstract

Background: *In drug-refractory heart failure, cardiac resynchronization therapy (CRT) is an established method in patients with sinus rhythm, severe reduced ejection fraction and broad QRS. Heart failure is known as a predisposition for atrial fibrillation (AF). However, the putative impact of atrioventricular node (AVN) ablation in chronic AF and CRT remains unclear. The aim of this study was to elucidate the effects of CRT in patients with chronic AF and the requirement for AVN ablation.*

Methods: *A total of 100 patients were included in the retrospective study, 64 with sinus rhythm (SR) and 36 with chronic AF with a mean duration of 2.8 ± 0.5 years. Clinical parameters, QRS duration and echocardiographic parameters were compared at baseline and after a follow-up of 11 ± 0.34 months in patients with SR and in 27 patients with chronic AF who received optimized medication to control ventricular rate and nine patients who underwent an AVN ablation.*

Results: *Baseline characteristics between patients with SR or AF in the presence or absence of AVN ablation were comparable. In each group, a significant improvement of NYHA class, ejection fraction could be observed, with an analogous reduction of QRS duration and a diminished left ventricular end-diastolic dimension after 11 ± 0.34 months of CRT.*

Conclusions: *The present results demonstrate a comparable improvement in left ventricular function and functional capacity in all treated groups. In conclusion, AVN ablation is not a prerequisite for CRT in patients with severe heart failure and chronic AF. (Cardiol J 2009; 16, 3: 246–249)*

Key words: cardiac resynchronization, atrial fibrillation, atrioventricular node ablation

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Introduction

Cardiac resynchronization therapy (CRT) is an established method for drug-refractory heart failure in patients with severe reduced ejection fraction and broad QRS configuration [1, 2]. Most clinical studies deal with CRT in patients with sinus rhythm [1–4]. On the other hand, heart failure predisposes the development of atrial fibrillation (AF) by atrial dilatation, structural changes in the myocardium and activation of the neuro-hormonal system [5].

The prevalence of AF in patients with heart failure varies between 10% and 25% for New York Heart Association (NYHA) class II to III and approximately 50% in NYHA class IV [6]. There is growing evidence that the benefit of CRT in patients with chronic AF and heart failure is similar to that in patients with sinus rhythm [7]. Effective suppression of rapid intrinsic atrio-ventricular conduction in patients with AF is mandatory to prevent incomplete biventricular capture and inhibition of CRT. It is well known that pharmacological treatment to control ventricular rate may be sufficient in patients with AF of short duration or with paroxysmal AF [8]. However, the putative improvement of atrio-ventricular node (AVN) ablation versus pharmacologic therapy in chronic AF and biventricular resynchronization therapy remains unclear.

The aim of this present study was to elucidate the effects of CRT in patients with chronic AF and the requirement of AVN ablation, comparing clinical and echocardiographic results.

Methods

A total of 100 patients were included in the retrospective study, 64 with sinus rhythm (SR), 36 with chronic AF with a mean duration of 2.8 ± 0.5 years. All patients suffered from drug-refractory heart failure with NYHA class III–IV, left ventricular ejection fraction (LVEF) $< 35\%$, QRS duration > 120 ms and left bundle branch block. Each patient had a left ventricular pacing lead in the lateral or posterolateral vein region, in the high right atrium and in the right ventricle. All patients were on an optimal medical heart failure regime. To produce a pharmacological blockade of atrio-ventricular conduction in AF, beta-blockers, digoxin and amiodarone were used, in order to ensure biventricular stimulation and regular left ventricular contraction. Two thirds of patients with chronic atrial fibrillation had a medication with amiodarone (Table 1).

Table 1. Basal characteristics in patients with chronic atrial fibrillation (AF) and chronic AF with atrioventricular node ablation (AVNA). There were no significant changes of medical heart failure regime over the follow-up of 11 ± 0.34 months. There was also no significant difference in medical treatment between the two groups.

	AF (n = 36)	AF with AVNA (n = 9)
ACE inhibitor	34 (94%)	8 (89%)
Beta-blocker	35 (97%)	8 (89%)
Diuretic	27 (75%)	9 (100%)
Spironolactone	12 (33%)	3 (33%)
Amiodarone	13 (36%)	1 (11%)
Digoxin	19 (53%)	4 (44%)

Retrospective follow-up and clinical evaluation were performed after 11 ± 0.34 months. The NYHA classification of heart failure symptoms was used. NYHA class, QRS duration and echocardiographic parameters were compared in patients with SR (group 1, n = 64) and in 27 patients (group 2) with chronic AF who received optimized medication to control ventricular rate, thus resulting in adequate delivery of biventricular pacing (biventricular stimulation $> 90\%$) and nine patients (group 3) who underwent an AVN ablation.

The study was approved by the local bioethical committee and all patients gave their informed consent.

Statistical analysis

All data are given as means \pm standard error of the mean (SEM). Data were compared with Student's t test for paired and unpaired data. Simultaneous comparisons between groups were carried out by means of one-way analysis of variance followed by Bonferroni's *post hoc* test when three or more groups were compared. For all tests, a p value < 0.05 was considered statistically significant.

Results

The study population comprised 64 patients with SR, 27 patients with chronic AF and nine patients with AVN ablation, a total of 86 men and 14 women (mean age 70 ± 7 years). The underlying disease was ischemic cardiomyopathy in 68 patients and nonischemic (dilatative) cardiomyopathy in 32 patients. Baseline characteristics between patients with SR or AF in the presence or absence of AVN ablation were comparable, whereas patients

Table 2. Characteristics of patients with sinus rhythm (SR), chronic atrial fibrillation (AF) and chronic AF with atrioventricular node ablation (AVNA) at baseline and after a follow-up of 11 ± 0.34 months. All data are given as means \pm standard error of the mean (SEM).

	SR (n = 64)		AF (n = 27)		AF with AVNA (n = 9)	
	Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up
NYHA class	3.1 ± 0.1	$1.9 \pm 0.1^*$	3.2 ± 0.1	$2.2 \pm 0.1^{††}$	3.2 ± 0.1	$2.3 \pm 0.2^{\ddagger}$
QRS [ms]	171.9 ± 3.7	$146.3 \pm 3.7^*$	189.5 ± 5.2	$156.7 \pm 3.5^{††}$	177.8 ± 6.8	$134.4 \pm 5.2^{\ddagger}$
LVEF (%)	24.6 ± 1.1	$34.7 \pm 1.4^*$	23.7 ± 1.2	$40.0 \pm 1.8^{††}$	24.4 ± 2.7	$37.9 \pm 3.4^{\ddagger}$
LVEDD [mm]	67.8 ± 1.1	$61.4 \pm 1.3^*$	69.7 ± 1.5	$62.9 \pm 1.4^{\ddagger}$	66.3 ± 1.9	$56.2 \pm 2.1^{\ddagger}$

*p < 0.01 versus baseline SR, ††p < 0.01 and †p < 0.05 versus baseline AF, ‡p < 0.05 versus baseline AF with AVNA. Follow-up SR versus follow-up AF and versus follow-up AF with AVNA; p = non significant; NYHA — New York Heart Association, LVEF — left ventricular ejection fraction, LVEDD — left ventricular end-diastolic dimension

with AF had significant larger left atrial dimensions. In patients with SR (group 1) mean NYHA class decreased from 3.1 ± 0.1 to 1.9 ± 0.1 ($p < 0.01$) and QRS duration decreased from 171.9 ± 3.7 ms to 146.3 ± 3.7 ms ($p < 0.01$) after 11 ± 0.34 months of CRT. Left ventricular ejection fraction increased significantly from $24.6 \pm 1.1\%$ to $34.7 \pm 1.4\%$ ($p < 0.01$) and left ventricular end-diastolic dimension (LVEDD) decreased from 67.8 ± 1.1 mm to 61.4 ± 1.3 mm ($p < 0.01$) during follow up (Table 2).

In patients with chronic AF (group 2), mean NYHA class decreased from 3.2 ± 0.1 to 2.2 ± 0.1 ($p < 0.01$). The broad QRS decreased from 189.5 ± 5.2 ms to 156.7 ± 3.5 ms ($p < 0.01$). After 11 ± 0.34 months of CRT the LVEF augmented from $23.7 \pm 1.2\%$ to $40.0 \pm 1.8\%$ ($p < 0.01$) and LVEDD diminished from 69.7 ± 1.5 mm to 62.9 ± 1.4 mm ($p < 0.05$) (Table 2).

In patients with chronic AF who had AVN ablation (group 3), mean NYHA class (3.2 ± 0.1 vs. 2.3 ± 0.2 ; $p < 0.01$), QRS duration (177.8 ± 6.8 ms vs. 134.4 ± 5.2 ms; $p < 0.05$) and LVEDD (66.3 ± 1.9 mm vs. 56.2 ± 2.1 mm; $p < 0.05$) decreased in response to CRT in a comparable manner to the group with AF and pharmacological treatment. There was also an analogous improvement in LVEF ($24.4 \pm 2.7\%$ vs. $37.9 \pm 3.4\%$; $p < 0.05$) after 11 ± 0.34 months of CRT (Table 2).

In the AF group with and without AVN ablation, left atrial dimensions were larger as in the SR group. There was no significant alteration in left atrial size in patients with SR (45.9 ± 0.8 mm vs. 42.9 ± 0.9 mm) or AF with (52.1 ± 2.3 mm vs. 51.4 ± 2.3 mm) or without (52.0 ± 1.0 mm vs. 49.9 ± 1.3 mm) AVN ablation after CRT treatment.

Discussion

In this study we assessed the role of CRT in patients with chronic AF and the requirement of

AVN ablation, comparing clinical and echocardiographic results.

The benefits of CRT in respect of NYHA class and LVEF improvement as well as reduction of QRS duration and LVEDD after follow-up of 11 ± 0.34 months were comparable. These findings are in accordance with previous results showing an improvement in clinical and echocardiographic parameters in patients with drug-refractory heart failure and CRT [1–6]. Recent studies have been almost exclusively restricted to patients with stable sinus rhythm [1–4]. However, the prevalence of AF in patients with heart failure and NYHA class II to IV varies between 25% and 50% [6]. There is growing evidence that the benefit in patients with chronic AF and heart failure is similar to that in patients with sinus rhythm [7]. A few studies have shown an acute improvement in hemodynamic response in patients with chronic AF immediately after CRT [9, 10]. The role of AVN ablation in patients with chronic AF versus optimal pharmacological treatment remains unclear. Recent results suggest a pharmacological therapy to control ventricular rate may be sufficient in patients with AF of short duration or paroxysmal AF [6]. Our study indicates a benefit and improvement of clinical parameters (NYHA) as well as echocardiographic results (LVEF, LVEDD) of CRT also in patients with chronic AF with a mean duration of 2.8 ± 0.5 years, but CRT had no effect on enlarged atrial dimensions in patients with AF with or without AVN ablation.

Our results accord with data from Molhoek et al. [11] who demonstrated a comparable benefit from CRT in patients with chronic AF compared to those who had SR. Corresponding data from Dorszewski et al. [12] showed a comparable improvement over a long-term follow-up in left ventricular function and exercise capacity in patients with chronic AF and optimized medical treatment. In contrast, results from Gasparini et al. [13] suggested a high

percentage of inadequate biventricular capture in patients with pharmacological treatment in AF and CRT. In this study, long-term improvements of left ventricular function and functional capacity were only observed if AVN ablation was performed. We achieved an adequate delivery of biventricular pacing (biventricular stimulation > 90%) in patients who received an optimized medication to control ventricular rate in chronic AF.

Comparing patients with chronic AF without AVN ablation against patients with AF who had AVN ablation, improvement of NYHA class, LVEF as well as decreased QRS duration and LVEDD were similar. This suggests that a sufficient rate control is the successful therapy option for the majority of patients with chronic AF and indication for CRT. Therefore, AVN ablation is not a precondition for cardiac resynchronization in patients with severe heart failure and chronic atrial fibrillation.

Limitations of the study

Several limitations apply to the present study. First, it had a relatively small sample size. Also, the precise duration of chronic AF before CRT is unknown and no data about annual hospitalization and long-term survival exist.

Conclusions

In conclusion, our results show a comparable improvement in left ventricular function and functional capacity in all treated groups, whereas an AVN ablation is not a prerequisite for cardiac resynchronization in patients with severe heart failure and chronic AF.

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References

1. Abraham WT, Fisher WG, Smith AL et al. MIRACLE Study Group. Cardiac resynchronization in chronic heart failure. *N Engl J Med*, 2002; 346: 1845–1853.
2. Jeevanantham V, Zareba W, Navaneethan S et al. Metaanalysis on effects of cardiac resynchronization therapy in heart failure patients with narrow QRS complex. *Cardiol J*, 2008; 15: 230–236.
3. Bristow MR, Saxon LA, Boehmer J et al. Comparison of medical therapy, pacing, and defibrillation in heart failure (COMPANION) Investigators. Cardiac resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. *N Engl J Med*, 2004; 350: 2140–2150.
4. Linde C, Leclercq C, Rex S et al. Long-term benefits of biventricular pacing in congestive heart failure: Results from the multisite stimulation in cardiomyopathy (MUSTIC) study. *J Am Coll Cardiol*, 2002; 40: 111–118.
5. Maisel WH, Stevenson LW. Atrial fibrillation in heart failure: epidemiology, pathophysiology, and rationale for therapy. *Am J Cardiol*, 2003; 91: 2–8.
6. Daubert JC. Introduction to atrial fibrillation and heart failure: A mutually noxious association. *Europace*, 2004; 5 (suppl. 1): S1–S4.
7. Delnoy PP, Ottervanger JP, Luttikhuis HO et al. Comparison of usefulness of cardiac resynchronization therapy in patients with atrial fibrillation and heart failure versus patients with sinus rhythm and heart failure. *Am J Cardiol*, 2007; 99: 1252–1257.
8. Hoppe UC. Resynchronization therapy in the context of atrial fibrillation: Benefits and limitations. *J Interv Card Electrophysiol*, 2007; 18: 225–232.
9. Hay I, Melenovsky V, Fetis BJ et al. Short-term effects of right-left heart sequential cardiac resynchronization in patients with heart failure, chronic atrial fibrillation, and atrioventricular nodal block. *Circulation*, 2004; 110: 3404–3410.
10. Etienne Y, Mansourati J, Gilard M et al. Evaluation of left ventricular based pacing in patients with congestive heart failure and atrial fibrillation. *Am J Cardiol*, 1999; 83: 1138–1140.
11. Molhoek SG, Bax JJ, Bleeker GB et al. Comparison of response to cardiac resynchronization therapy in patients with sinus rhythm versus chronic atrial fibrillation. *Am J Cardiol*, 2004; 94: 1506–1509.
12. Dorszewski A, Berndt C, Lamp B et al. Langzeitergebnis chronisch herzinsuffizienter Patienten mit Vorhofflimmern nach Resynchronisationstherapie ohne AV-Knoten-Ablation. *Clin Res Cardiol*, 2007; 96: Suppl 1.
13. Gasparini M, Auricchio A, Regoli F et al. Four-year efficacy of cardiac resynchronization therapy on exercise tolerance and disease progression: The importance of performing atrioventricular junction ablation in patients with atrial fibrillation. *J Am Coll Cardiol*, 2006; 48: 734–743.